vascular closure devices, with no complications (Figure). General anesthesia was used in 2 patients because of their age.

For percutaneous closure of the fistulas (video 1 of the supplementary material), we used 4-Fr to 7-Fr introducers for the femoral vein and artery. Using a hydrophilic guidewire through a guiding catheter, the fistula was crossed from the LCA toward the inferior vena cava and externalized through the venous side. An Amplatzer Vascular Plug, sized according to the size of the fistula (Table), was implanted from the venous side (retrograde approach) through a multipurpose guiding catheter in the first patient and the Amplatzer delivery system in the second patient. In the third patient, the device was advanced and implanted through a 5-Fr JR guiding catheter from the arterial side of the fistula (anterograde approach) (Table).

In the CTA images performed at completion of each procedure, the devices proved to be adequately positioned, with minimal residual flow toward the fistulas and preserved flow toward the LCA (video 2 of the supplementary material).

The patients received dual oral antiplatelet therapy with no loading dose, consisting of 81 mg of aspirin and 75 mg of clopidogrel for 6 months, and thereafter, only aspirin to decrease the risk of device thrombosis, which might affect the LCA and right chambers. Later CTA studies showed an absence of flow through the coronary fistulas toward the atria, with adequate positioning of the devices.

Most patients with this condition are asymptomatic, although some have dyspnea, arrhythmia, ischemia secondary to coronary steal, fistula rupture or thrombosis, infective endocarditis due to turbulent flow, or edema of the lower limbs caused by the volume overload resulting from the left to right shunt. The diagnosis can be made by echocardiography, but the fistula is better characterized by CTA, which is recommended to help plan the best treatment strategy, either percutaneous or surgical.

The guidelines recommend closing the fistula if it produces symptoms, regardless of the size,[4] but particularly when it is large, being arbitrarily considered as such when the fistula segment is at least 3-fold greater than the diameter of the normal coronary artery.[5]

Closure using a percutaneous procedure is recommended for fistulas that are not multiple and not excessively tortuous, in patients who do not require another type of cardiac intervention. Closure is usually successful with the use of several types of devices.[6] As to the technique, implanting the device as far distally as possible has been proposed to avoid ischemia resulting from occlusion of the vessel of origin or one of its branches.[6] In our patients, we decided to use vascular closure devices because they have the advantages of easy implantation, a large range of sizes, and the possibility to safely reposition the device during and after placement.

The procedure can be performed using an anterograde or retrograde technique. In the cases presented, both these approaches were used, depending on the patients' anatomical characteristics. The size of the device was calculated based on the coronary CTA findings and the angiography findings during the procedure.

The outcome of this case series shows that successful percutaneous closure of large, somewhat complex fistulas is now possible.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at: http://dx.doi.org/10.1016/j.recesp.2016.08.023.

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Transcatheter Aortic Valve Implantation in Patients With Previous Mitral Prostheses

Implante percutáneo de válvula aórtica en pacientes con prótesis mitral previa

To the Editor,

Transcatheter aortic valve implantation (TAVI) is an established intervention with a growing number of indications. TAVI is increasingly used in patients with a history of heart surgery because of the high estimated cardiovascular risk in this patient subgroup. An especially interesting situation is presented by patients with a previous mitral prosthesis (PMP). The potential for interaction between the TAVI device and the PMP increases procedural complexity, and it is therefore very important from a clinical standpoint to evaluate the experience accumulated to date with these patients. The aim of this systematic review was to examine all published evidence on TAVI in patients with a PMP. An exhaustive literature search was conducted of PUBMED, EMBASE, and the Cochrane Library using the following search terms: "transcatheter", "percutaneous", "aortic valve intervention" and/or "replacement" and "previous mitral intervention", "surgery", "replacement" and/or "prostheses". We then conducted a descrip-

tive analysis of the total number of patients (N = 97) and a univariate analysis to identify predictors of complications among those patients for whom individual data were reported (n = 57).

A total of 97 patients were identified in 24 articles published between 2008[1] and 2016 (Table of the Supplementary material); the patient population included the series published by Barbanti et al.[2] The mean age of the population was 75. 5 ± 9.6 years (range, 31-93 years) and 80.4% were women. Of the total, 34% of patients had severe ventricular dysfunction and 95% were in New York Heart Association functional class III-IV. Mean surgical risk according to the Society of Thoracic Surgeons (STS) score was 16.6% ± 13.8% (range, 3.3%-75%); 72.4% of patients were at high risk and 27.6% were at intermediate risk. The mean interval between mitral intervention and TAVI was 14.5 ± 5.6 years (range, 2-28 years). The aortic valve prosthesis was mechanical in 80.4% of patients and biological in 17.5%; the remaining 2.1% of patients received only a prosthetic annulus. The approach used was transfemoral in 57 patients (58.5%), transapical in 33, transaortic in 4, and transaxillary in 3. Preprocedure valvuloplasty was carried out in 94.9% of patients and was used to determine the risk of PMP interaction by transesophageal echocardiography in 81.6%. The following devices were implanted: CoreValve (Medtronic, Minnesotta, United States) in 50 patients; Edwards SAPIEN (Edwards Lifesciences, Irvine, California, United States) in 44 patients; and ACURATE TA (Symetis, Ecublens, Switzerland), Engager (Medtronic, Minnesota, United States), and JenaValve (JenaValve Technology GmbH, Germany) in 1 patient each.

In-hospital complications were recorded in 19.8% of patients, with major bleeding in 11.3% and PMP interaction in 7.2%. In 1 patient, PMP interaction caused rapid hemodynamic deterioration requiring traction of the valve to the ascending aorta; in another, it produced severe aortic failure, which was resolved by sequential postdilatation; and in a third patient, the interaction necessitated elective open surgery. Other complications were the need to fit a pacemaker (1%), endocarditis (1%), and intraprocedural stroke (1%). Among patients for whom individual data were available (n = 57), we determined the predictors of these complications (excluding the need for a definitive pacemaker, which appeared to be underreported). The main factors showing an association are listed in the Table. Of the complications, 50% were related to interaction with the PMP ($P < .001$), which was associated with a lower procedure success rate according to Valve Academic Research Consortium (VARC-2) criteria (50% vs 100%; $P < .001$). All cases of PMP interaction involved a self-expanding aortic prosthesis ($P = .053$ compared with other percutaneous prostheses). Although the type of mitral prosthesis showed no statistical association with interaction, 5 of the 6 complications occurred in patients with a mechanical mitral prosthesis (80% of them double-disk and 20% of another kind; $P = .638$).

Interaction of the TAVI device with a PMP was thus infrequent (affecting ∼3% of patients), occurred mostly with mechanical mitral prostheses, and appeared to be more common with double disk prostheses. Another factor associated with interaction was the use of self-expanding aortic prostheses, which protrude further into the left ventricular outflow tract; this finding would therefore suggest that, in the absence of other indications, balloon-expandable devices should be the first choice. Retrievable devices and other new devices with alternative release mechanisms have so far generated insufficient data to support conclusions, and therefore extreme caution should be exercised in the use of such devices in patients with a PMP. To date, better results in this patient subgroup appear to be achieved when TAVI is performed with a balloon-expandable prosthesis.

Table
Baseline Characteristics of TAVI Patients With a Previous Mitral Prosthesis, Grouped According to In-hospital Complications

Variables	Total Population (n = 57)	Without complications (n = 51)	With complications (n = 6)	*P*
Women	49/56 (86)	44/50 (88)	5/6 (83.3)	.569
Age, y	75 ± 10	75 ± 9	71 ± 17	.376
LVEF, %	50 [30-60]	50 [30-60]	55 [30-60]	.723
NYHA III-IV/IV	46/46 (100)	40/40 (100)	6/6 (100)	.999
STS score (%)	11 [7.5-26.5]	10 [6.9-29.2]	17.1 [11.0-23.0]	.217
Type of mitral prosthesis				
Mechanical	48/57 (84.2)	43/51 (84.3)	5/6 (83.3)	.999
Dual-disk	24/37 (64.8)	20/32 (62.5)	4/5 (80)	.638
Other[a]	13/37 (35.2)	12/32 (37.5)	1/5 (20)	
Approach				
Transfemoral	28/57 (49.1)	25/51 (49)	3/6 (50)	
Transapical	27/57 (47.4)	25/51 (49)	2/6 (33.3)	.315
Other[b]	2/57 (3.5)	1/51 (2)	1/6 (16.7)	
Previous aortic valvuloplasty	37/39 (94.9)	35/37 (94.7)	2/2 (100)	0,999
Type of TAVI				
CoreValve	22/57 (38.6)	18/51 (35.3)	4/6 (66.7)	.192
Other[c]	35/57 (61.4)	33/51 (64.7)	2/6 (33.3)	
General anesthesia	35/43 (81.4)	32/39 (82.1)	3/4 (75)	.999
TEE guidance	40/49 (81.6)	37/45 (82.2)	3/4 (75)	.569
Success (VARC-2)	54/57 (94.7)	51/51 (100)	3/6 (50)	.001
PMP interaction	3/57 (5.3)	0	3/6 (50)	.001

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class; PMP, previous mitral prosthesis; TAVI, transcatheter aortic valve implantation; TEE, transesophageal echocardiography; VARC, Valve Academic Research Consortium.
Normally distributed quantitative variables are presented as mean ± standard deviation (comparison with the Student *t* test), and nonnormally distributed variables as median [interquartile range] (comparison with the Mann-Whitney *U* test). Qualitative data are presented as n/N (%) and comparisons were made with the chi-square test or the Fisher exact test.

[a] Monodisk (n = 10), ball-cage (n = 2), other (1).
[b] Transaortic (n = 1), transubclavian (n = 1).
[c] Edwards Sapien XT (32), Acurate (n = 1), Enganger (n = 1), Jena Valve (n = 1).

Despite the relative infrequency of interaction between a TAVI prosthesis and a PMP, this problem caused 50% of in-hospital complications (excluding conduction disorders) and a significant decrease in TAVI success rate according to VARC-2 criteria; however, in general this complication could be resolved satisfactorily during the intervention.

A clear publication bias exists in this area, and there is therefore a need for larger series and ideally randomized studies to evaluate the best approach to use in this technically challenging patient subgroup. Regardless of this consideration, careful planning of these interventions should include computed tomography and other imaging studies to determine the distance between the prosthesis and the aortic ring ($\geq$ 3 mm for the transapical route and 7 mm for the transfemoral route).[3] Furthermore, intraprocedural transesophageal echocardiography can reduce the risk of this worrisome complication, independently of the specific TAVI approach used.

SUPPLEMENTARY MATERIAL

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Hypertrophic Cardiomyopathy Without Ventricular Hypertrophy: Usefulness of Genetic and Pathological Study in Preventing Sudden Death

Miocardiopatía hipertrófica sin hipertrofia ventricular: utilidad del estudio anatomopatológico y genético en la prevención de la muerte súbita

To the Editor,

Hypertrophic cardiomyopathy (HCM) is diagnosed by the presence of ventricular hypertrophy $\geq$ 15 mm in the absence of any abnormal loading conditions that could cause it, or $\geq$ 13 mm if a relative is known to have HCM. On histological examination, myofibrillar disarray is characteristic of the disease. However, there have been reports of cases of HCM with sudden death (SD) in which the only identified abnormalities were myofibrillar disarray or mutations in the *TNNT2* gene.[1] We present a family with multiple cases of SD, in which pathological examination and genetic study were key in the diagnosis.

The proband was a 28-year-old woman, with no past medical history of note, who died suddenly while getting into her car. Postmortem examination revealed a heart weighing 295 g with a 13-mm interventricular septum. Microscopic examination showed microscopic fiber hypertrophy and isolated foci of myofibrillar disarray (Figure 1B). Family history included 4 maternal aunts of the proband who had SD at the ages of 17 (n = 2), 18, and 30 years (Figure 1A). The proband's 55-year-old mother had a normal echocardiogram and an electrocardiogram (ECG) with repolarization abnormalities in the inferolateral leads. The proband had 3 sisters and 1 brother, with different fathers. One of the sisters, aged 30 years, had a completely normal echocardiogram and cardiac magnetic resonance (CMR) scan, but ECG showed ST depression in the inferolateral leads. Stress echocardiography and coronary angiography showed no abnormalities. The other 2 sisters had normal echocardiograms and ECGs. In the brother, mild left ventricular hypertrophy was observed, with a 16-mm interventricular septum, and the ECG showed abnormalities similar to those of the sister and the mother (Table 1).

Given the suspicion of familial HCM with mild phenotypic expression and the high incidence of SD, a genetic study was performed on a frozen blood sample from the deceased patient. We used a panel that identifies, through next-generation sequencing, multiple genes associated with cardiomyopathies and channelopathies, given the possibility of an underlying channelopathy in the deceased patients. An Arg94Leu mutation was identified in the troponin T gene (*TNNT2*). This mutation was first described in a British family with a high prevalence of premature SD ($<$ 45 years old) and a diagnosis compatible with HCM. The patients had no history of illness, with SD being the first clinical manifestation. Postmortem examination revealed the absence of macroscopic hypertrophy, although histological examination showed diffuse fibrosis and myocyte disarray. In fact, that study was one of the first to establish that mutations in *TNNT2* could be associated with SD even in the absence of overt hypertrophy.[2,3] Two other mutations affecting the same residue have been described (Arg94Cys, Arg94His) and therefore it appears to be a point susceptible to mutations. This would suggest that any change in the amino acid sequence at this point would be poorly-tolerated. The clinical information available on carriers of these mutations agrees with other findings, such as the recently-published observations on the Arg92Gln mutation in several Mallorcan families.[4] Some studies evaluating microscopic examination in carriers of troponin T mutations indicate that these cause less hypertrophy and fibrosis, but more disarray, than other sarcomere mutations. This could be the underlying factor that explains the high risk of arrhythmia.[5]

The genetic study of the rest of the family showed that the mother, 1 sister (and her 2 children), and the brother (and 1 of his daughters) were carriers of the identified mutation. The latest guidelines do not recommend automatic cardioverter-defibrillator implantation for the presence of a single mutation; however, a defibrillator was implanted as prevention in the proband's 2 carrier siblings, aged 33 and 35 years, due to patient preference (no risk factors except family history of SD) (Table 1). The other carriers,